EMA/264176/2023

European Medicines Agency decision

P/0240/2023

of 14 June 2023

on the acceptance of a modification of an agreed paediatric investigation plan for givinostat (EMEA-000551-PIP04-21-M02) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0062/2022 issued on 11 March 2022 and the decision P/0513/2022 issued on 4 December 2022,

Having regard to the application submitted by Italfarmaco S.p.A. on 20 March 2023 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 26 May 2023, in accordance with Article 22 of Regulation (EC) No 1901/2006,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for givinostat, oral suspension, oral use, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision is addressed to Italfarmaco S.p.A., Via dei Lavoratori, 54, 20092 - Cinisello Balsamo (Milan), Italy.

EMA/PDCO/153098/2023 Corr[1]
Amsterdam, 26 May 2023

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-000551-PIP04-21-M02

Scope of the application

Active substance(s):

Givinostat

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of Duchenne muscular dystrophy

Pharmaceutical form(s):

Oral suspension

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Italfarmaco S.p.A.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Italfarmaco S.p.A. submitted to the European Medicines Agency on 20 March 2023 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0062/2022 issued on 11 March 2022 and the decision P/0513/2022 issued on 4 December 2022.

The application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 24 April 2023.

[1] 8 June 2023

Scope of the modification

Some measures of the Paediatric Investigation Plan have been modified.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan in the scope set out in the Annex I of this opinion;

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition:

Treatment of Duchenne muscular dystrophy.

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- oral suspension, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric investigation plan

2.1. Condition:

Treatment of Duchenne muscular dystrophy

2.1.1. Indication(s) targeted by the PIP

Treatment of Duchenne muscular dystrophy (DMD)

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 2 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Oral suspension

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Assessment of the suitability of the oral suspension formulation, of intragastric administration via feeding tubes.
Non-clinical studies	**Study 2** Safety study of givinostat in juvenile rats from post-natal day (PND)7.
Clinical studies	**Study 3** 2-part open-label study to assess the safety, tolerability, pharmacokinetics (PK), effects on histology and clinical parameters of givinostat in ambulant paediatric patients from 7 years to less than 11 years of age with DMD (DSC/11/2357/43).

	Study 4 Randomised, double-blind safety and efficacy study of givinostat versus placebo in ambulant paediatric patients from 6 years to less than 18 years of age with DMD (DSC/14/2357/48). **Study 5** Randomised, double-blind safety and efficacy study of givinostat versus placebo in non-ambulant paediatric patients from 9 years to less than 18 years of age with DMD (DSC/14/2357/50). **Study 6** Open-label, long term safety study of givinostat in paediatric patients from 6 years to less than 18 years of age with DMD (DSC/14/2357/51). **Study 7** Open-label, safety and pharmacokinetic study of givinostat in paediatric patients from 2 years to less than 6 years of age with DMD (DSC/14/2357/52).
Extrapolation, modelling and simulation studies	**Study 8** Population pharmacokinetic (PK) model to support dose rationale of givinostat in paediatric patients with DMD. **Study 9** Population pharmacokinetic (PK)-pharmacodynamic (PD) model to estimate the risk of experiencing a reduction in platelets in DMD patients treated with givinostat. **Study 10** Population pharmacokinetic (PK)-pharmacodynamic (PD) model to correlate clinical parameters with PK data in DMD patients treated with givinostat. **Study 11** Analysis of existing in-house pharmacokinetic (PK)/pharmacodynamic (PD) data and literature data on givinostat in the treatment of DMD to support extrapolation of efficacy data in patients with DMD younger than 6 years of age. **Study 12** Population pharmacokinetic (PK)-pharmacodynamic (PD) model to correlate clinical parameters with PK data in DMD patients treated with givinostat.
Other studies	Not applicable.
Other measures	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By March 2026
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

The product is not authorised anywhere in the European Community.